

Abstract No. Chan0125

Fimbrin Structure

M. Klein, S. Almo (AECOM)

Beamline(s): X9A

Protein Name: Fimbrin

Organism: *Arabidopsis thaliana*

PDB Code: to be deposited

Rationale for Target Selection: The structure of the entire actin crosslinking core of a fimbrin molecule has not been described. Two of the four calponin homology (CH) domains show less than 30% identity with all previously described CH domains.

Method of Structure Determination: Initial 3.0 Å map was generated by three wavelength Se-met MAD experiment at NSLS X9B. Previously characterized human fimbrin CH subdomains were rapidly positioned in the map by use of our six dimensional phased translation function (<http://russel.bioc.aecom.yu.edu/server/NYSGRC.html>). Data were subsequently extended to 2.2 Å at X9A and the R-factor(R-free) is 22% (27%).

Structure Description: This structure represents the full actin crosslinking core, containing the two actin binding domains (ABD), each of which is composed of two tandemly repeated CH subdomains (for a total of four CH subdomains in the entire core). As previously observed in an isolated the single human fimbrin ABD, CH1 and CH2, and CH3 and CH4 pack to form an ABD. Remarkably, the two ABDs pack to form a single compact globular unit.

Comparisons of Structurally Similar Proteins in PDB: A DALI search shows that plant CH3 is most closely related to human fimbrin CH1 (1AOA, 21% identity, z-score=15.3, RMS=1.7Å) and the CH from calponin (1H67, 23% identity, z-score 12.2, RMS 2.1Å); and that the plant CH4 is most similar to human fimbrin CH1 (1AOA, 16% identity, z-score=13.9, RMS=2.3Å) and the CH from alpha-spectrin (1BKR, 23% identity, z-score 13.5, RMS 2.2Å).

Results of Comparative Protein Structure Modeling: In progress

Biological Implications: The two independent copies of the core in the asymmetric are generally similar, but there are considerable differences in the detailed packing between individual CH subdomains within a given ABD. This suggests that the ABDs are rather dynamic structures, perhaps as a consequence of structural rearrangements that accompany formation of an actin bundle. In addition, within the core, the two ABDs pack along an extensive interface that is inconsistent with previously predicted models. Furthermore, this interface contains a number of highly conserved residues previously thought to be involved in actin binding. Our structural observations suggest that the entire mechanism of fimbrin function needs to be reconsidered.

Value for the PSI: Further expands the structural coverage of the biologically important class of CH domains and highlights the utility of the six dimensional phased translation function for aiding in fitting an experimental electron density map. This structure also highlights the importance of examining multidomain proteins containing individual domains exhibiting less than 30% identity with a PDB entry, despite the fact that the entire protein might exhibit greater than 30%.

Lessons for the NYSGRC:

Great utility of the six dimensional phased translation function.